UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
CHEMICAL SAFETY
AND POLLUTION

November 27, 2012
Revised Review on May 21, 2013

MEMORANDUM

SUBJECT: Efficacy Review for Technical Sodium Chlorite;
EPA Reg. No. 88341-R;
DP Barcode: D405203

FROM: Karen M. Hill, Ph.D.
Microbiologist
Efficacy Evaluation Team
Product Science Branch
Antimicrobials Division (7510P)

K. Hill 5/21/13

THRU: Mark Perry
Team Leader
Product Science Branch
Antimicrobials Division (7510P)

MP

TO: Monisha Harris RM32/ David Liem
Regulatory Management Branch II
Antimicrobials Division (7510P)

APPLICANT: T.A. Combs
4196 Merchant Plaza #344
Lake Ridge, VA 22192

Formulation from the Label:

Active Ingredient(s):	% by wt.
Sodium Chlorite*	31%
Inert Ingredients	69%
Total	100%

* Available Chlorine- 24%

I. BACKGROUND:

The product, Technical Sodium Chlorite (EPA Reg. No. 88341-R), is seeking registration as disinfectant for water use only in commercial and institutional environments. The application is a re-submission in response to an Agency letter dated 10/13/11. Studies were conducted at ATS Labs, located at 1285 Corporate Center Drive, Suite 110, in Eagan, MN 55121. The applicant responded to the deficiencies noted in previous review. This review is in response to the applicant's submission of information addressing the unacceptable findings in the previous efficacy evaluation report.

This data package contained a letter from the applicant's representative to EPA dated August 03, 2012 (MRID 489041-00), EPA Form 8570-4 (CSF), two studies (MRID 489041-06 and 489041-07), proposed label, and Statement of No Data Confidentiality Claims for both studies.

II. USE DIRECTIONS:

The product is designed for disinfection use in water including re-circulating cooling water towers, mechanical or electrolytic generators of chlorine dioxide, potable water treatment, industrial cooling water treatment, mollusk control in water systems, food plant process water treatment, wastewater treatment, paper mills, poultry processing water, oil wells, and petroleum systems.

Directions on the proposed label provide the following information regarding use of the product as a disinfectant for potable water treatment:

Chlorine dioxide is used as both an oxidant and a disinfectant in drinking water treatment. The required dosages will vary with source water conditions and the degree of contamination present. For most municipal and public potable water systems, a chlorine dioxide residual concentration of up to 2 ppm is sufficient to provide adequate disinfection. Residual disinfectant byproducts must be monitored as required by the National Primary Drinking Water Regulation (40 CFR Part 141) and state drinking water standards.

Directions on the proposed label provide the following information regarding use of the product as a disinfectant for food plant process water treatment:

Chlorine dioxide generated from sodium chlorite is effective for use in controlling microbiological growth in flume water and other food processing water systems such as chill water systems and hydro coolers. The required dosages will vary with process conditions and the degree of contamination present. Depending on the requirements of the specific water system, sodium chlorite should be applied continuously or intermittently through a chlorine dioxide generating system to achieve a chlorine dioxide residual concentration between 0.25 and 5.0 ppm.

Water containing up to 3 ppm residual chlorine dioxide may be used for washing fruits and vegetables that are not raw agricultural commodities in accordance with 21CFR§173.300. Treatment of the fruits and vegetables with chlorine dioxide must be followed by a potable water rinse, or by blanching, cooking or canning.

Chlorine dioxide gas may be used for fumigating fruits and vegetables that are not raw agricultural commodities in accordance with 21CFR§173.300. Treatment of the fruits and vegetables with chlorine dioxide in a closed chamber system must be followed by a potable water rinse, or by blanching, cooking or canning.

Directions on the proposed label provide the following information regarding use of the product as a disinfectant for waste water treatment:

Chlorine dioxide is used as both an oxidant and a disinfectant in drinking water treatment. The required dosages will vary with source water conditions and the degree of contamination present. For most municipal and public potable water systems, a chlorine dioxide residual concentration of up to 5 ppm is sufficient to provide adequate disinfection.

For sulfide odor control, between pH 5 – 9, a minimum of 5.2 ppm (wt.) of chlorine dioxide should be applied to oxidize 1 ppm of sulfide (measured as sulfide ion). For phenol destruction, at pH less than 8, 1.5 ppm chlorine dioxide will oxidize 1 ppm phenol; at pH greater than 10, 3.3 ppm chlorine dioxide will oxidize 1 ppm phenol.

Directions on the proposed label provide the following information regarding use of the product as a disinfectant for poultry processing water:

Chlorine dioxide generated from this product may be used as an antimicrobial agent in water used in poultry processing, provided that the residual concentration of chlorine dioxide does not exceed 3 ppm, as determined by an appropriate method in accordance with 21CFR§173.300.

For treatment of poultry chill water, apply this product as necessary through a chlorine dioxide generation system to maintain a residual concentration of up to 3 parts per million (ppm) chlorine dioxide in the chiller water.

Directions on the proposed label provide the following information regarding use of the product as a disinfectant for oil wells and petroleum systems:

Chlorine dioxide is effective in the remediation of bacterial and sulfide contamination commonly found in oilfield production, injection, and disposal fluids. The required dosages will vary with process conditions. Sodium chlorite may be applied either continuously or intermittently through a chlorine dioxide generating system to oil well production water as it is separated from the oil, and before it is re-injected into the well.

For continuous feeds, chlorine dioxide may be applied at dosages slightly higher than sulfide's oxidative demand as determined by a demand study. For intermittent treatment, chlorine dioxide should be applied at a shock dosage of 200 – 3000 ppm.

III. AGENCY STANDARDS FOR PROPOSED CLAIMS:

Products for Treating Water Systems (Emergency water supplies or Water purifier):

These requirements apply to chemical additives such as solutions, powders, or tablets intended for emergency purification of small quantities of drinking water of questionable potability, by the general public, in the absence of bacteriological monitoring facilities. Three samples of product, representing three batches, one of which should be at least 60 days aged, should be tested in triplicate. The "recommended

test method" is "Guide Standard and Protocol for Testing Microbiological Water Purifiers - Section 3." This reference is a general guide and in some cases may present only the minimum features and framework for the testing of microbiological water purifiers. However, the principles and approaches outlined in this reference should provide initial guidance for the testing of various types of units and/or systems for the microbiological purification of contaminated water.

Products must be tested and demonstrated to meet the following microbiological reduction requirements:

- Bacteria: A 6-log (99.9999%) reduction of an influent challenge of 10^7 organisms per 100 mL of the bacterial challenge organism, *Raoultella terrigena* (ATCC 33257).

- Viruses: A 4-log (99.99%) reduction of a mixed influent challenge of 10^7 organisms per liter of each of the following viruses: Poliovirus (LSc) (ATCC VR-59) and Rotavirus (WA or SA-11) (ATCC VR-899 or VR-2018). [Virus types are to be mixed in roughly equal 1 x 10^7/L concentrations and a joint 4 log reduction will be acceptable.]

IV. COMMENTS ON THE SUBMITTED EFFICACY STUDY:

1. MRID 489041-06 "Test Method for Disinfectants for Use in Water," Test Organism: *Raoultella terrigena* (ATCC 33257), for product Technical Sodium Chlorite, by Anne Stemper. Study conducted at ATS Labs 1285 Corporate Center Drive Suite 110 Eagen, MN. 55121. Study completion date – August 3, 2012. Project Identification Number A13273.

The study was conducted against *Raoultella terrigena* (ATCC 33257). Three lots of pure chlorine dioxide stock solution (31% Technical Sodium Chlorite), Lots 20111025, Lot 20120204A, and Lot 20120204B, of the product were tested using the provided ATS Laboratory Protocol No. CWA01122911.CUST.2 marked as proprietary Information. The product lots testing substance were prepared by the sponsor, Lot 20120204A concentration of chlorine dioxide was 350 ppm, Lot 20120204B concentration of chlorine dioxide was 296 ppm, and Lot 20111025 concentration of chlorine dioxide was 755 ppm. For each lot, on the day of testing the sponsor prepared the test substance by bubbling nitrogen gas through the pure chlorine dioxide stock solution and the endpoint determined visually. The sponsor determined the actual chlorine dioxide concentration for each lot by titration and the value (296 – 755 ppm) was used to prepare the 2 ppm chlorine dioxide concentration used in testing. A culture of the challenge microorganism was prepared by streaking an appropriate number of Tryptic Soy + 5% Sheep Blood Agar plates using a stock culture and incubating the plates for 2 days at 35 – 37°C aerobically. Following incubation, the test organism was transferred to Butterfield's Buffer to yield a uniform culture suspension that was adjusted as needed to match a 4.0 McFarland standard. The test water (EPA #2) was prepared by adding 0.60 g sample of dry-autoclaved ISO A2 fine test dust to 500 mL of deionized water and shaken vigorously. In addition, 1.10 g sample of Spectrum humic acid was added to the suspension and shaken vigorously prior to addition of 40 g sample of Sigma sea salts that were mixed vigorously until dissolved. The well mixed suspension was added to a large vessel containing deionized water and mixed thoroughly. The pH of the final test water solution was adjusted as necessary using 10 drops of NaOH to a final pH of 9.04 and the temperature of the EPA #2 water was maintained at 4 ± 1°C (3.5°C) during

testing using a water bath set at the desired temperature. The EPA #2 water was prepared within one week of use in testing and was stored at 2 – 8°C. One liter (1000mL) of EPA# 2 test water was inoculated with 2 mL of prepared test organism to target ≥1 X 10^5 CFU per mL or ≥1 X 10^8 CFU per liter and mixed well to ensure the test organism suspension was evenly dispersed. For Lot 20120204A, a 6 mL aliquot of test substance was added to an inoculated vessel of EPA #2 test water. For Lot 20120204B, a 7 mL aliquot of test substance was added to an inoculated vessel of EPA #2 test water. For Lot 20111025, a 3 mL aliquot of test substance was added to an inoculated vessel of EPA #2 test water. Each sample was thoroughly mixed and allowed to be exposed for 60 minutes at 4 ± 1°C (3.5°C). Two individual 100 mL aliquots of exposed test substance were transferred to vessels containing 10 mL of appropriate neutralizer (0.1 N Sodium Thiosulfate) and mixed. The neutralized sample was filtered through a sterile 0.45 µm filter apparatus system. The filter was rinsed, aseptically removed, and transferred to the surface of Tryptic Soy + 5% Sheep Blood Agar. All subculture plates were incubated for 48 ± 4 hours at 35 – 37°C and stored at 2 – 8°C for three days prior to visual examination for the presence or absence of growth. Controls included purity, sterility, initial suspension population, and neutralization.

2. MRID 489041-07 "Test Method for Disinfectants for the Evaluation of a Water Treatment Product to Reduce Poliovirus type 1 and Rotavirus in Point -of- Use Water," Test Organism: Poliovirus type 1 (ATCC VR 1562) and Rotavirus (University of Ottawa, Ontario Canada), for product Technical Sodium Chlorite, by Mary J. Miller. Study conducted at ATS Labs 1285 Corporate Center Drive Suite 110 Eagen, MN. 55121. Study completion date – July 25, 2012. Project Identification Number A13266.

The study was conducted against Poliovirus type 1, Strain Chat (ATCC VR 1562) and Rotavirus, strain WA (University of Ottawa, Ontario Canada). Rhesus monkey kidney (MA-104) cells were used as the host cell line for both test viruses. Three lots of pure chlorine dioxide stock solution (31% Technical Sodium Chlorite), Lots 20111025, Lot 20120204A, and Lot 20120204B, of the product were tested using the provided ATS Laboratory Protocol No. CWA01122911.CUST.2 marked as proprietary Information. The product lots were received as stock sodium chlorite solutions and added to water for a final concentration of 2 ppm chlorine dioxide for testing. The stock viruses were prepared by collecting the supernatant culture fluid from 75 - 100% infected culture cells that were disrupted and cell debris removed by centrifugation. The high titer stock virus supernatant for each virus were aliquoted and stored at ≤-70°C until the day of use then fifteen (15) aliquots of stock virus for Poliovirus type 1 (ATS Labs Lot PC2-18) and fifteen (15) aliquots of stock virus for Rotavirus (ATS Labs Lot XR-140) were removed, thawed, combined, and maintained at a refrigerated temperature until used in the assay. The test water (EPA #2) was prepared by adding 0.60 g sample of dry-autoclaved ISO A2 fine test dust to 500 mL of deionized water and shaken vigorously. In addition, 1.10 g sample of Spectrum humic acid was added to the suspension and shaken vigorously prior to addition of 40 g sample of Sigma sea salts that were mixed vigorously until dissolved. The well mixed suspension was added to a large vessel containing deionized water and mixed thoroughly. The pH of the final test water solution was adjusted as necessary using 10 drops of NaOH to a final pH of 9.04 and the temperature of the EPA #2 water was maintained at 4 ± 1°C (3.5°C) during testing using a water bath set at the desired temperature. The EPA #2 water was prepared within one week of use in testing and was stored at 2 – 8°C. One liter (1000mL) of EPA# 2 test water for each viral (Rotavirus and Poliovirus type 1) testing were inoculated with 5 mL of virus that had

a minimum titer of approximately 1 X 10^7 $TCID_{50}$/mL and mixed well to ensure the test organism suspension was evenly dispersed. Ten-fold serial dilutions were performed from a 5 mL aliquot of the inoculated water to determine the level of virus contained in test water. For Lot 20120204A, a 6 mL aliquot of test substance was added to an inoculated vessel of EPA #2 test water for each virus. For Lot 20120204B, a 7 mL aliquot of test substance was added to an inoculated vessel of EPA #2 test water for each virus. For Lot 20111025, a 3 mL aliquot of test substance was added to an inoculated vessel of EPA #2 test water for each virus. Each sample was thoroughly mixed and allowed to be exposed for 60 minutes at 4°C. Two individual 10 mL aliquots of exposed test substance were transferred to vessels containing 100 mL of appropriate neutralizer (0.1 N Sodium Thiosulfate) and mixed. Ten-fold (10) serial dilutions were prepared. MA-104 cells in multi well (12 well) culture plates were inoculated in quadruplicate with 1000 µL aliquots of the dilutions prepared from the test and control groups. All subculture plates were incubated at 36 – 38°C with 5 – 7% CO_2 humidified atmosphere. The cultures were score periodically for seven days for the absence or presence of cytopathy, cytotoxicity, and viability. Controls included input virus control, initial virus control, cytotoxicity, and neutralization. Titers were calculated using the Spearman Karber method.

V. RESULTS:

MRID Number	Organism	Geometric Mean and Average Log_{10}			Initial Suspension Population Control Log (CFU/L)
		Lot 20120204A	Lot 20120204B	Lot 20111025	
	60-Minute Exposure Time				
489041-06	*Raoultella terrigena*	<1.00 <0.00	<1.00 <0.00	<1.00 <0.00	1.11×10^9
	Percent Reduction	>99.999999	>99.9999999	>99.9999999	
	Log_{10} Reduction	>8.87	>9.04	>9.23	

MRID Number	Organism	Average $TCID_{50}$/ 1000µL (Log)			Initial Virus Control Average Log_{10} ($TCID_{50}$/1000µL)
		Lot 20120204A	Lot 20120204B	Lot 20111025	
	60-Minute Exposure Time				
489041-07	Poliovirus type 1	$10^{1.07}$	$10^{1.00}$	$10^{1.07}$	$\geq 10^{8.16}$
	Cytotoxicity	None	None	None	
	Joint Initial Control Average	$\geq 10^{8.17}$	$\geq 10^{8.17}$	$\geq 10^{8.17}$	
	Log_{10} Reduction	≥7.09	≥7.16	≥7.09	

MRID Number	Organism	Average $TCID_{50}$/ 1000µL (Log)			Initial Virus Control Average Log_{10} ($TCID_{50}$/1000µL)
		Lot 20120204A	Lot 20120204B	Lot 20111025	
		60-Minute Exposure Time			
489041-07	Rotavirus	$10^{1.39}$	$10^{1.52}$	$10^{1.52}$	$\geq 10^{6.55}$
	Cytotoxicity	None	None	None	
	Joint Initial Virus Control	$\geq 10^{8.17}$	$\geq 10^{8.17}$	$\geq 10^{8.17}$	
	Log_{10} Reduction	5.16	5.03	5.03	

VI. CONCLUSIONS:

1. The submitted efficacy data does support the use of the product, Technical Sodium Chlorite, as a disinfectant for use in water against the following microorganisms for a 60-minute contact time:

Raoultella terrigena	MRID 489041-06
Poliovirus type 1	MRID 489041-07
Rotavirus	MRID 489041-07

All of the tested lots were ≥60 days aged. A 6-log (99.9999%) reduction of an influent challenge of 10^7 organisms per 100 mL of the bacterial challenge organism, *Raoultella terrigena* (ATCC 33257) was demonstrated. A 4-log (99.99%) reduction of a mixed influent challenge of 10^7 organisms per liter of each of the following viruses: Poliovirus and Rotavirus (WA or SA-11) were demonstrated. For MRID 489041-06, purity controls showed pure, sterility controls did not have growth, and neutralization controls demonstrated growth. For MRID 489041-07, there was not any cytotoxicity seen and neutralization controls demonstrated growth.

VII. RECOMMENDATIONS:

1. The proposed label claims that the product, Technical Sodium Chlorite, is an effective disinfectant for use in potable water against the following microorganisms for a 60-minute contact time:

Raoultella terrigena	ATCC 33257
Poliovirus type 1	ATCC VR-1562
Rotavirus, Strain WA	University of Ottawa, Ontario Canada

These claims are **acceptable** as they are supported by the submitted data.

2. The following recommendations for the **Label** must be made:

- On page 4 under Potable Water Treatment: remove "For most municipal and potable water systems" and rewrite as "For municipal and potable water systems".

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revised & updated May 21, 2013. converted to 3/90 ai.

MEMORANDUM

SUBJECT: Efficacy Review for Technical Sodium Chlorite;
EPA Reg. No. 88341-R;
DP Barcode: D405203

FROM: Karen M. Hill, Ph.D.
Microbiologist
Efficacy Evaluation Team
Product Science Branch
Antimicrobials Division (7510P)

K. Hill 11/27/12

THRU: Emily Mitchell
Branch Chief
Product Science Branch
Antimicrobials Division (7510P)

for Emily

TO: Monisha Harris RM32/ David Liem
Regulatory Management Branch II
Antimicrobials Division (7510P)

APPLICANT: T.A. Combs
4196 Merchant Plaza #344
Lake Ridge, VA 22192

Formulation from the Label:

Active Ingredient(s):	% by wt.
Sodium Chlorite*.....	80%
Inert Ingredients.....	20%
Total.....	100%

* Available Chlorine- 125%

I. BACKGROUND:

The product, Technical Sodium Chlorite (EPA Reg. No. 88341-R), is seeking registration as disinfectant in commercial and institutional environments. The application is a re-submission in response to an Agency letter dated 10/13/11. Studies were conducted at ATS Labs, located at 1285 Corporate Center Drive, Suite 110, in Eagan, MN 55121.

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II. USE DIRECTIONS:

The product is designed for disinfection use in water including re-circulating cooling water towers, mechanical or electrolytic generators of chlorine dioxide, potable water treatment, industrial cooling water treatment, mollusk control in water systems, food plant process water treatment, wastewater treatment, paper mills, poultry processing water, oil wells, and petroleum systems.

Directions on the proposed label provide the following information regarding use of the product as a disinfectant for potable water treatment:

Chlorine dioxide is used as both an oxidant and a disinfectant in drinking water treatment. The required dosages will vary with source water conditions and the degree of contamination present. For most municipal and public potable water systems, a chlorine dioxide residual concentration of up to 2 ppm is sufficient to provide adequate disinfection. Residual disinfectant byproducts must be monitored as required by the National Primary Drinking Water Regulation (40 CFR Part 141) and state drinking water standards.

Directions on the proposed label provide the following information regarding use of the product as a disinfectant for food plant process water treatment:

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Water containing up to 3 ppm residual chlorine dioxide may be used for washing fruits and vegetables that are not raw agricultural commodities in accordance with 21CFR§173.300. Treatment of the fruits and vegetables with chlorine dioxide must be followed by a potable water rinse, or by blanching, cooking or canning.

Chlorine dioxide gas may be used for fumigating fruits and vegetables that are not raw agricultural commodities in accordance with 21CFR§173.300. Treatment of the fruits and vegetables with chlorine dioxide in a closed chamber system must be followed by a potable water rinse, or by blanching, cooking or canning.

Directions on the proposed label provide the following information regarding use of the product as a disinfectant for waste water treatment:

Chlorine dioxide is used as both an oxidant and a disinfectant in drinking water treatment. The required dosages will vary with source water conditions and the degree of contamination present. For most municipal and public potable water systems, a chlorine dioxide residual concentration of up to 5 ppm is sufficient to provide adequate disinfection.

For sulfide odor control, between pH 5 – 9, a minimum of 5.2 ppm (wt.) of chlorine dioxide should be applied to oxidize 1 ppm of sulfide (measured as sulfide ion). For phenol destruction, at pH less than 8, 1.5 ppm chlorine dioxide will oxidize 1 ppm phenol; at pH greater than 10, 3.3 ppm chlorine dioxide will oxidize 1 ppm phenol.

Directions on the proposed label provide the following information regarding use of the product as a disinfectant for poultry processing water:

Chlorine dioxide generated from this product may be used as an antimicrobial agent in water used in poultry processing, provided that the residual concentration of chlorine dioxide does not exceed 3 ppm, as determined by an appropriate method in accordance with 21CFR§173.300.

For treatment of poultry chill water, apply this product as necessary through a chlorine dioxide generation system to maintain a residual concentration of up to 3 parts per million (ppm) chlorine dioxide in the chiller water.

Directions on the proposed label provide the following information regarding use of the product as a disinfectant for oil wells and petroleum systems:

Chlorine dioxide is effective in the remediation of bacterial and sulfide contamination commonly found in oilfield production, injection, and disposal fluids. The required dosages will vary with process conditions. Sodium chlorite may be applied either continuously or intermittently through a chlorine dioxide generating system to oil well production water as it is separated from the oil, and before it is re-injected into the well.

For continuous feeds, chlorine dioxide may be applied at dosages slightly higher than sulfide's oxidative demand as determined by a demand study. For intermittent treatment, chlorine dioxide should be applied at a shock dosage of 200 – 3000 ppm.

III. AGENCY STANDARDS FOR PROPOSED CLAIMS:

Products for Treating Water Systems (Emergency water supplies or Water purifier):

These requirements apply to chemical additives such as solutions, powders, or tablets intended for emergency purification of small quantities of drinking water of questionable potability, by the general public, in the absence of bacteriological monitoring facilities. Three samples of product, representing three batches, one of which should be at least 60 days aged, should be tested in triplicate. The "recommended test method" is "Guide Standard and Protocol for Testing Microbiological Water Purifiers - Section 3." This reference is a general guide and in some cases may present only the minimum features and framework for the testing of microbiological water purifiers. However, the principles and approaches outlined in this reference should provide initial

guidance for the testing of various types of units and/or systems for the microbiological purification of contaminated water.

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- Viruses: A 4-log (99.99%) reduction of a mixed influent challenge of 10^7 organisms per liter of each of the following viruses: Poliovirus (LSc) (ATCC VR-59) and Rotavirus (WA or SA-11) (ATCC VR-899 or VR-2018). [Virus types are to be mixed in roughly equal 1 x 10^7/L concentrations and a joint 4 log reduction will be acceptable.]

IV. COMMENTS ON THE SUBMITTED EFFICACY STUDY:

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substance was added to an inoculated vessel of EPA #2 test water. For Lot 20120204B, a 7 mL aliquot of test substance was added to an inoculated vessel of EPA #2 test water. For Lot 20111025, a 3 mL aliquot of test substance was added to an inoculated vessel of EPA #2 test water. Each sample was thoroughly mixed and allowed to be exposed for 60 minutes at 4 ± 1°C (3.5°C). Two individual 100 mL aliquots of exposed test substance were transferred to vessels containing 10 mL of appropriate neutralizer (0.1 N Sodium Thiosulfate) and mixed. The neutralized sample was filtered through a sterile 0.45 µm filter apparatus system. The filter was rinsed, aseptically removed, and transferred to the surface of Tryptic Soy + 5% Sheep Blood Agar. All subculture plates were incubated for 48 ± 4 hours at 35 – 37°C and stored at 2 – 8°C for three days prior to visual examination for the presence or absence of growth. Controls included purity, sterility, initial suspension population, and neutralization.

2. MRID 489041-07 "Test Method for Disinfectants for the Evaluation of a Water Treatment Product to Reduce Poliovirus type 1 and Rotavirus in Point -of- Use Water," Test Organism: Poliovirus type 1 (ATCC VR 1562) and Rotavirus (University of Ottawa, Ontario Canada), for product Technical Sodium Chlorite, by Mary J. Miller. Study conducted at ATS Labs 1285 Corporate Center Drive Suite 110 Eagen, MN. 55121. Study completion date – July 25, 2012. Project Identification Number A13266.

This study was conducted against Poliovirus type 1, Strain Chat (ATCC VR 1562) and Rotavirus, strain WA (University of Ottawa, Ontario Canada). Rhesus monkey kidney (MA-104) cells were used as the host cell line for both test viruses. Three lots of pure chlorine dioxide stock solution (31% Technical Sodium Chlorite), Lots 20111025, Lot 20120204A, and Lot 20120204B, of the product were tested using the provided ATS Laboratory Protocol No. CWA01122911.CUST.2 marked as proprietary Information. The product lots were received as stock sodium chlorite solutions and added to water for a final concentration of 2 ppm chlorine dioxide for testing. The stock viruses were prepared by collecting the supernatant culture fluid from 75 - 100% infected culture cells that were disrupted and cell debris removed by centrifugation. The high titer stock virus supernatant for each virus were aliquoted and stored at ≤-70°C until the day of use then fifteen (15) aliquots of stock virus for Poliovirus type 1 (ATS Labs Lot PC2-18) and fifteen (15) aliquots of stock virus for Rotavirus (ATS Labs Lot XR-140) were removed, thawed, combined, and maintained at a refrigerated temperature until used in the assay. The test water (EPA #2) was prepared by adding 0.60 g sample of dry-autoclaved ISO A2 fine test dust to 500 mL of deionized water and shaken vigorously. In addition, 1.10 g sample of Spectrum humic acid was added to the suspension and shaken vigorously prior to addition of 40 g sample of Sigma sea salts that were mixed vigorously until dissolved. The well mixed suspension was added to a large vessel containing deionized water and mixed thoroughly. The pH of the final test water solution was adjusted as necessary using 10 drops of NaOH to a final pH of 9.04 and the temperature of the EPA #2 water was maintained at 4 ± 1°C (3.5°C) during testing using a water bath set at the desired temperature. The EPA #2 water was prepared within one week of use in testing and was stored at 2 – 8°C. One liter (1000mL) of EPA# 2 test water for each viral (Rotavirus and Poliovirus type 1) testing were inoculated with 5 mL of virus that had a minimum titer of approximately 1 X 10^7 $TCID_{50}$/mL and mixed well to ensure the test organism suspension was evenly dispersed. Ten-fold serial dilutions were performed from a 5 mL aliquot of the inoculated water to determine the level of virus contained in test water. For Lot 20120204A, a 6 mL aliquot of test substance was added to an inoculated vessel of EPA #2 test water for each virus. For Lot 20120204B,

a 7 mL aliquot of test substance was added to an inoculated vessel of EPA #2 test water for each virus. For Lot 20111025, a 3 mL aliquot of test substance was added to an inoculated vessel of EPA #2 test water for each virus. Each sample was thoroughly mixed and allowed to be exposed for 60 minutes at 4°C. Two individual 10 mL aliquots of exposed test substance were transferred to vessels containing 100 mL of appropriate neutralizer (0.1 N Sodium Thiosulfate) and mixed. Ten-fold (10) serial dilutions were prepared. MA-104 cells in multi well (12 well) culture plates were inoculated in quadruplicate with 1000 µL aliquots of the dilutions prepared from the test and control groups. All subculture plates were incubated at 36 – 38°C with 5 – 7% CO_2 humidified atmosphere. The cultures were score periodically for seven days for the absence or presence of cytopathy, cytotoxicity, and viability. Controls included input virus control, initial virus control, cytotoxicity, and neutralization. Titers were calculated using the Spearman Karber method.

V. RESULTS:

MRID Number	Organism	Geometric Mean and Average Log_{10}			Initial Suspension Population Control Log (CFU/L)
		Lot 20120204A	Lot 20120204B	Lot 20111025	
	60-Minute Exposure Time				
489041-06	*Raoultella terrigena*	<1.00 <0.00	<1.00 <0.00	<1.00 <0.00	1.11×10^9
	Percent Reduction	>99.999999	>99.9999999	>99.9999999	
	Log_{10} Reduction	>8.87	>9.04	>9.23	

MRID Number	Organism	Average $TCID_{50}$/ 1000µL (Log)			Initial Virus Control Average Log_{10} ($TCID_{50}$/1000µL)
		Lot 20120204A	Lot 20120204B	Lot 20111025	
	60-Minute Exposure Time				
489041-07	Poliovirus type 1	$10^{1.07}$	$10^{1.00}$	$10^{1.07}$	$\geq 10^{8.16}$
	Cytotoxicity	None	None	None	
	Joint Initial Control Average	$\geq 10^{8.17}$	$\geq 10^{8.17}$	$\geq 10^{8.17}$	
	Log_{10} Reduction	≥7.09	≥7.16	≥7.09	

MRID Number	Organism	Average $TCID_{50}$/ 1000µL (Log)			Initial Virus Control Average Log_{10} ($TCID_{50}$/1000µL)
		Lot 20120204A	Lot 20120204B	Lot 20111025	
	60-Minute Exposure Time				
489041-07	Rotavirus	$10^{1.39}$	$10^{1.52}$	$10^{1.52}$	$\geq 10^{6.55}$
	Cytotoxicity	None	None	None	
	Joint Initial Virus Control	$\geq 10^{8.17}$	$\geq 10^{8.17}$	$\geq 10^{8.17}$	
	Log_{10} Reduction	5.16	5.03	5.03	

VI. CONCLUSIONS:

1. The submitted efficacy data do not support the use of the product, Technical Sodium Chlorite, as a disinfectant for use in water against the following microorganisms for a 60-minute contact time:

Raoultella terrigena	MRID 489041-06
Poliovirus type 1	MRID 489041-07
Rotavirus	MRID 489041-07

A Lot ≥60 days aged was not tested or clearly indicated in any of the submitted studies. The product identity tested, Pure Chlorine Dioxide Solution (31% Technical Sodium Chlorite), was not confirmed as the product seeking registration, Technical Sodium Chlorite 80% tablet. A 6-log (99.9999%) reduction of an influent challenge of 10^7 organisms per 100 mL of the bacterial challenge organism, *Raoultella terrigena* (ATCC 33257) was demonstrated. A 4-log (99.99%) reduction of a mixed influent challenge of 10^7 organisms per liter of each of the following viruses: Poliovirus and Rotavirus (WA or SA-11) was demonstrated. For MRID 489041-06, purity controls showed pure, sterility controls did not have growth, and neutralization controls demonstrated growth. For MRID 489041-07, there was not any cytotoxicity seen and neutralization controls demonstrated growth.

VII. RECOMMENDATIONS:

1. The proposed label claims that the product, Technical Sodium Chlorite, is an effective disinfectant for use in water against the following microorganisms for a 60-minute contact time:

Raoultella terrigena	ATCC 33257
Poliovirus type 1	ATCC VR-1562
Rotavirus, Strain WA	University of Ottawa, Ontario Canada

These claims are **unacceptable** as they are not supported by the submitted data.

2. The following recommendations for the **Label** must be made:

- The dilution rate must be indicated. Directions for use must include the dilution of the product needed to accomplish the indicated ppm for each usage.
- In order to add claims using the registration eligibility decision (RED), an available chlorine test must be performed to determine the product equivalence to the established ppm level that demonstrates efficacy for RED claims.

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

OFFICE OF
CHEMICAL SAFETY
AND POLLUTION

November 27, 2012

MEMORANDUM

SUBJECT: Efficacy Review for Technical Sodium Chlorite;
EPA Reg. No. 88341-R;
DP Barcode: D405203

FROM: Karen M. Hill, Ph.D.
Microbiologist
Efficacy Evaluation Team
Product Science Branch
Antimicrobials Division (7510P)

K. Hill 11/27/12

THRU: Emily Mitchell
Branch Chief
Product Science Branch
Antimicrobials Division (7510P)

for Emily

TO: Monisha Harris RM32/ David Liem
Regulatory Management Branch II
Antimicrobials Division (7510P)

APPLICANT: T.A. Combs
4196 Merchant Plaza #344
Lake Ridge, VA 22192

Formulation from the Label:

Active Ingredient(s):	% by wt.
Sodium Chlorite*.....	80%
Inert Ingredients.....	20%
Total.....	100%

* Available Chlorine- 125%

I. BACKGROUND:

The product, Technical Sodium Chlorite (EPA Reg. No. 88341-R), is seeking registration as disinfectant in commercial and institutional environments. The application is a re-submission in response to an Agency letter dated 10/13/11. Studies were conducted at ATS Labs, located at 1285 Corporate Center Drive, Suite 110, in Eagan, MN 55121.

This data package contained a letter from the applicant's representative to EPA dated August 03, 2012 (MRID 489041-00), EPA Form 8570-4 (CSF), two studies (MRID 489041-06 and 489041-07), proposed label, and Statement of No Data Confidentiality Claims for both studies.

II. USE DIRECTIONS:

The product is designed for disinfection use in water including re-circulating cooling water towers, mechanical or electrolytic generators of chlorine dioxide, potable water treatment, industrial cooling water treatment, mollusk control in water systems, food plant process water treatment, wastewater treatment, paper mills, poultry processing water, oil wells, and petroleum systems.

Directions on the proposed label provide the following information regarding use of the product as a disinfectant for potable water treatment:

Chlorine dioxide is used as both an oxidant and a disinfectant in drinking water treatment. The required dosages will vary with source water conditions and the degree of contamination present. For most municipal and public potable water systems, a chlorine dioxide residual concentration of up to 2 ppm is sufficient to provide adequate disinfection. Residual disinfectant byproducts must be monitored as required by the National Primary Drinking Water Regulation (40 CFR Part 141) and state drinking water standards.

Directions on the proposed label provide the following information regarding use of the product as a disinfectant for food plant process water treatment:

Chlorine dioxide generated from sodium chlorite is effective for use in controlling microbiological growth in flume water and other food processing water systems such as chill water systems and hydro coolers. The required dosages will vary with process conditions and the degree of contamination present. Depending on the requirements of the specific water system, sodium chlorite should be applied continuously or intermittently through a chlorine dioxide generating system to achieve a chlorine dioxide residual concentration between 0.25 and 5.0 ppm.

Water containing up to 3 ppm residual chlorine dioxide may be used for washing fruits and vegetables that are not raw agricultural commodities in accordance with 21CFR§173.300. Treatment of the fruits and vegetables with chlorine dioxide must be followed by a potable water rinse, or by blanching, cooking or canning.

Chlorine dioxide gas may be used for fumigating fruits and vegetables that are not raw agricultural commodities in accordance with 21CFR§173.300. Treatment of the fruits and vegetables with chlorine dioxide in a closed chamber system must be followed by a potable water rinse, or by blanching, cooking or canning.

Directions on the proposed label provide the following information regarding use of the product as a disinfectant for waste water treatment:

Chlorine dioxide is used as both an oxidant and a disinfectant in drinking water treatment. The required dosages will vary with source water conditions and the degree of contamination present. For most municipal and public potable water systems, a chlorine dioxide residual concentration of up to 5 ppm is sufficient to provide adequate disinfection.

For sulfide odor control, between pH 5 – 9, a minimum of 5.2 ppm (wt.) of chlorine dioxide should be applied to oxidize 1 ppm of sulfide (measured as sulfide ion). For phenol destruction, at pH less than 8, 1.5 ppm chlorine dioxide will oxidize 1 ppm phenol; at pH greater than 10, 3.3 ppm chlorine dioxide will oxidize 1 ppm phenol.

Directions on the proposed label provide the following information regarding use of the product as a disinfectant for poultry processing water:

Chlorine dioxide generated from this product may be used as an antimicrobial agent in water used in poultry processing, provided that the residual concentration of chlorine dioxide does not exceed 3 ppm, as determined by an appropriate method in accordance with 21CFR§173.300.

For treatment of poultry chill water, apply this product as necessary through a chlorine dioxide generation system to maintain a residual concentration of up to 3 parts per million (ppm) chlorine dioxide in the chiller water.

Directions on the proposed label provide the following information regarding use of the product as a disinfectant for oil wells and petroleum systems:

Chlorine dioxide is effective in the remediation of bacterial and sulfide contamination commonly found in oilfield production, injection, and disposal fluids. The required dosages will vary with process conditions. Sodium chlorite may be applied either continuously or intermittently through a chlorine dioxide generating system to oil well production water as it is separated from the oil, and before it is re-injected into the well.

For continuous feeds, chlorine dioxide may be applied at dosages slightly higher than sulfide's oxidative demand as determined by a demand study. For intermittent treatment, chlorine dioxide should be applied at a shock dosage of 200 – 3000 ppm.

III. AGENCY STANDARDS FOR PROPOSED CLAIMS:

Products for Treating Water Systems (Emergency water supplies or Water purifier):

These requirements apply to chemical additives such as solutions, powders, or tablets intended for emergency purification of small quantities of drinking water of questionable potability, by the general public, in the absence of bacteriological monitoring facilities. Three samples of product, representing three batches, one of which should be at least 60 days aged, should be tested in triplicate. The "recommended test method" is "Guide Standard and Protocol for Testing Microbiological Water Purifiers - Section 3." This reference is a general guide and in some cases may present only the minimum features and framework for the testing of microbiological water purifiers. However, the principles and approaches outlined in this reference should provide initial

guidance for the testing of various types of units and/or systems for the microbiological purification of contaminated water.

Products must be tested and demonstrated to meet the following microbiological reduction requirements:

- Bacteria: A 6-log (99.9999%) reduction of an influent challenge of 10^7 organisms per 100 mL of the bacterial challenge organism, *Raoultella terrigena* (ATCC 33257).

- Viruses: A 4-log (99.99%) reduction of a mixed influent challenge of 10^7 organisms per liter of each of the following viruses: Poliovirus (LSc) (ATCC VR-59) and Rotavirus (WA or SA-11) (ATCC VR-899 or VR-2018). [Virus types are to be mixed in roughly equal 1 x 10^7/L concentrations and a joint 4 log reduction will be acceptable.]

IV. COMMENTS ON THE SUBMITTED EFFICACY STUDY:

1. MRID 489041-06 "Test Method for Disinfectants for Use in Water," Test Organism: *Raoultella terrigena* (ATCC 33257), for product Technical Sodium Chlorite, by Anne Stemper. Study conducted at ATS Labs 1285 Corporate Center Drive Suite 110 Eagen, MN. 55121. Study completion date – August 3, 2012. Project Identification Number A13273.

This study was conducted against *Raoultella terrigena* (ATCC 33257). Three lots of pure chlorine dioxide stock solution (31% Technical Sodium Chlorite), Lots 20111025, Lot 20120204A, and Lot 20120204B, of the product were tested using the provided ATS Laboratory Protocol No. CWA01122911.CUST.2 marked as proprietary Information. The product lots testing substance were prepared by the sponsor, Lot 20120204A concentration of chlorine dioxide was 350 ppm, Lot 20120204B concentration of chlorine dioxide was 296 ppm, and Lot 20111025 concentration of chlorine dioxide was 755 ppm. For each lot, on the day of testing the sponsor prepared the test substance by bubbling nitrogen gas through the pure chlorine dioxide stock solution and the endpoint determined visually. The sponsor determined the actual chlorine dioxide concentration for each lot by titration and the value (296 – 755 ppm) was used to prepare the 2 ppm chlorine dioxide concentration used in testing. A culture of the challenge microorganism was prepared by streaking an appropriate number of Tryptic Soy + 5% Sheep Blood Agar plates using a stock culture and incubating the plates for 2 days at 35 – 37°C aerobically. Following incubation, the test organism was transferred to Butterfield's Buffer to yield a uniform culture suspension that was adjusted as needed to match a 4.0 McFarland standard. The test water (EPA #2) was prepared by adding 0.60 g sample of dry-autoclaved ISO A2 fine test dust to 500 mL of deionized water and shaken vigorously. In addition, 1.10 g sample of Spectrum humic acid was added to the suspension and shaken vigorously prior to addition of 40 g sample of Sigma sea salts that were mixed vigorously until dissolved. The well mixed suspension was added to a large vessel containing deionized water and mixed thoroughly. The pH of the final test water solution was adjusted as necessary using 10 drops of NaOH to a final pH of 9.04 and the temperature of the EPA #2 water was maintained at 4 ± 1°C (3.5°C) during testing using a water bath set at the desired temperature. The EPA #2 water was prepared within one week of use in testing and was stored at 2 – 8°C. One liter (1000mL) of EPA# 2 test water was inoculated with 2 mL of prepared test organism to target ≥1 X 10^5 CFU per mL or ≥1 X 10^8 CFU per liter and mixed well to ensure the test organism suspension was evenly dispersed. For Lot 20120204A, a 6 mL aliquot of test

substance was added to an inoculated vessel of EPA #2 test water. For Lot 20120204B, a 7 mL aliquot of test substance was added to an inoculated vessel of EPA #2 test water. For Lot 20111025, a 3 mL aliquot of test substance was added to an inoculated vessel of EPA #2 test water. Each sample was thoroughly mixed and allowed to be exposed for 60 minutes at 4 ± 1°C (3.5°C). Two individual 100 mL aliquots of exposed test substance were transferred to vessels containing 10 mL of appropriate neutralizer (0.1 N Sodium Thiosulfate) and mixed. The neutralized sample was filtered through a sterile 0.45 µm filter apparatus system. The filter was rinsed, aseptically removed, and transferred to the surface of Tryptic Soy + 5% Sheep Blood Agar. All subculture plates were incubated for 48 ± 4 hours at 35 – 37°C and stored at 2 – 8°C for three days prior to visual examination for the presence or absence of growth. Controls included purity, sterility, initial suspension population, and neutralization.

2. MRID 489041-07 "Test Method for Disinfectants for the Evaluation of a Water Treatment Product to Reduce Poliovirus type 1 and Rotavirus in Point -of- Use Water," Test Organism: Poliovirus type 1 (ATCC VR 1562) and Rotavirus (University of Ottawa, Ontario Canada), for product Technical Sodium Chlorite, by Mary J. Miller. Study conducted at ATS Labs 1285 Corporate Center Drive Suite 110 Eagen, MN. 55121. Study completion date – July 25, 2012. Project Identification Number A13266.

This study was conducted against Poliovirus type 1, Strain Chat (ATCC VR 1562) and Rotavirus, strain WA (University of Ottawa, Ontario Canada). Rhesus monkey kidney (MA-104) cells were used as the host cell line for both test viruses. Three lots of pure chlorine dioxide stock solution (31% Technical Sodium Chlorite), Lots 20111025, Lot 20120204A, and Lot 20120204B, of the product were tested using the provided ATS Laboratory Protocol No. CWA01122911.CUST.2 marked as proprietary Information. The product lots were received as stock sodium chlorite solutions and added to water for a final concentration of 2 ppm chlorine dioxide for testing. The stock viruses were prepared by collecting the supernatant culture fluid from 75 - 100% infected culture cells that were disrupted and cell debris removed by centrifugation. The high titer stock virus supernatant for each virus were aliquoted and stored at ≤-70°C until the day of use then fifteen (15) aliquots of stock virus for Poliovirus type 1 (ATS Labs Lot PC2-18) and fifteen (15) aliquots of stock virus for Rotavirus (ATS Labs Lot XR-140) were removed, thawed, combined, and maintained at a refrigerated temperature until used in the assay. The test water (EPA #2) was prepared by adding 0.60 g sample of dry-autoclaved ISO A2 fine test dust to 500 mL of deionized water and shaken vigorously. In addition, 1.10 g sample of Spectrum humic acid was added to the suspension and shaken vigorously prior to addition of 40 g sample of Sigma sea salts that were mixed vigorously until dissolved. The well mixed suspension was added to a large vessel containing deionized water and mixed thoroughly. The pH of the final test water solution was adjusted as necessary using 10 drops of NaOH to a final pH of 9.04 and the temperature of the EPA #2 water was maintained at 4 ± 1°C (3.5°C) during testing using a water bath set at the desired temperature. The EPA #2 water was prepared within one week of use in testing and was stored at 2 – 8°C. One liter (1000mL) of EPA# 2 test water for each viral (Rotavirus and Poliovirus type 1) testing were inoculated with 5 mL of virus that had a minimum titer of approximately 1 X 10^7 $TCID_{50}$/mL and mixed well to ensure the test organism suspension was evenly dispersed. Ten-fold serial dilutions were performed from a 5 mL aliquot of the inoculated water to determine the level of virus contained in test water. For Lot 20120204A, a 6 mL aliquot of test substance was added to an inoculated vessel of EPA #2 test water for each virus. For Lot 20120204B,

a 7 mL aliquot of test substance was added to an inoculated vessel of EPA #2 test water for each virus. For Lot 20111025, a 3 mL aliquot of test substance was added to an inoculated vessel of EPA #2 test water for each virus. Each sample was thoroughly mixed and allowed to be exposed for 60 minutes at 4°C. Two individual 10 mL aliquots of exposed test substance were transferred to vessels containing 100 mL of appropriate neutralizer (0.1 N Sodium Thiosulfate) and mixed. Ten-fold (10) serial dilutions were prepared. MA-104 cells in multi well (12 well) culture plates were inoculated in quadruplicate with 1000 µL aliquots of the dilutions prepared from the test and control groups. All subculture plates were incubated at 36 – 38°C with 5 – 7% CO_2 humidified atmosphere. The cultures were score periodically for seven days for the absence or presence of cytopathy, cytotoxicity, and viability. Controls included input virus control, initial virus control, cytotoxicity, and neutralization. Titers were calculated using the Spearman Karber method.

V. RESULTS:

MRID Number	Organism	Geometric Mean and Average Log_{10}			Initial Suspension Population Control Log (CFU/L)
		Lot 20120204A	Lot 20120204B	Lot 20111025	
	60-Minute Exposure Time				
489041-06	*Raoultella terrigena*	<1.00 <0.00	<1.00 <0.00	<1.00 <0.00	1.11×10^9
	Percent Reduction	>99.999999	>99.9999999	>99.9999999	
	Log_{10} Reduction	>8.87	>9.04	>9.23	

MRID Number	Organism	Average $TCID_{50}$/ 1000µL (Log)			Initial Virus Control Average Log_{10} ($TCID_{50}$/1000µL)
		Lot 20120204A	Lot 20120204B	Lot 20111025	
	60-Minute Exposure Time				
489041-07	Poliovirus type 1	$10^{1.07}$	$10^{1.00}$	$10^{1.07}$	$\geq 10^{8.16}$
	Cytotoxicity	None	None	None	
	Joint Initial Control Average	$\geq 10^{8.17}$	$\geq 10^{8.17}$	$\geq 10^{8.17}$	
	Log_{10} Reduction	≥7.09	≥7.16	≥7.09	

MRID Number	Organism	Average $TCID_{50}$/ 1000µL (Log)			Initial Virus Control Average Log_{10} ($TCID_{50}$/1000µL)
		Lot 20120204A	Lot 20120204B	Lot 20111025	
		60-Minute Exposure Time			
489041-07	Rotavirus	$10^{1.39}$	$10^{1.52}$	$10^{1.52}$	$\geq 10^{6.55}$
	Cytotoxicity	None	None	None	
	Joint Initial Virus Control	$\geq 10^{8.17}$	$\geq 10^{8.17}$	$\geq 10^{8.17}$	
	Log_{10} Reduction	5.16	5.03	5.03	

VI. CONCLUSIONS:

1. The submitted efficacy data do not support the use of the product, Technical Sodium Chlorite, as a disinfectant for use in water against the following microorganisms for a 60-minute contact time:

Raoultella terrigena	MRID 489041-06
Poliovirus type 1	MRID 489041-07
Rotavirus	MRID 489041-07

A Lot ≥60 days aged was not tested or clearly indicated in any of the submitted studies. The product identity tested, Pure Chlorine Dioxide Solution (31% Technical Sodium Chlorite), was not confirmed as the product seeking registration, Technical Sodium Chlorite 80% tablet. A 6-log (99.9999%) reduction of an influent challenge of 10^7 organisms per 100 mL of the bacterial challenge organism, *Raoultella terrigena* (ATCC 33257) was demonstrated. A 4-log (99.99%) reduction of a mixed influent challenge of 10^7 organisms per liter of each of the following viruses: Poliovirus and Rotavirus (WA or SA-11) was demonstrated. For MRID 489041-06, purity controls showed pure, sterility controls did not have growth, and neutralization controls demonstrated growth. For MRID 489041-07, there was not any cytotoxicity seen and neutralization controls demonstrated growth.

VII. RECOMMENDATIONS:

1. The proposed label claims that the product, Technical Sodium Chlorite, is an effective disinfectant for use in water against the following microorganisms for a 60-minute contact time:

Raoultella terrigena	ATCC 33257
Poliovirus type 1	ATCC VR-1562
Rotavirus, Strain WA	University of Ottawa, Ontario Canada

These claims are **unacceptable** as they are not supported by the submitted data.

2. The following recommendations for the **Label** must be made:

- The dilution rate must be indicated. Directions for use must include the dilution of the product needed to accomplish the indicated ppm for each usage.
- In order to add claims using the registration eligibility decision (RED), an available chlorine test must be performed to determine the product equivalence to the established ppm level that demonstrates efficacy for RED claims.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, DC 20460

80% a.i.

OFFICE OF
CHEMICAL SAFETY
AND POLLUTION

November 27, 2012

MEMORANDUM

SUBJECT: Efficacy Review for Technical Sodium Chlorite;
EPA Reg. No. 88341-R;
DP Barcode: D405203

FROM: Karen M. Hill, Ph.D.
Microbiologist
Efficacy Evaluation Team
Product Science Branch
Antimicrobials Division (7510P)

K. Hill 11/27/12

THRU: Emily Mitchell
Branch Chief
Product Science Branch
Antimicrobials Division (7510P)

for Emily

TO: Monisha Harris RM32/ David Liem
Regulatory Management Branch II
Antimicrobials Division (7510P)

APPLICANT: T.A. Combs
4196 Merchant Plaza #344
Lake Ridge, VA 22192

Formulation from the Label:

Active Ingredient(s):	% by wt.
Sodium Chlorite*.....	80%
Inert Ingredients.....	20%
Total.....	100%

* Available Chlorine- 125%

I. BACKGROUND:

The product, Technical Sodium Chlorite (EPA Reg. No. 88341-R), is seeking registration as disinfectant in commercial and institutional environments. The application is a re-submission in response to an Agency letter dated 10/13/11. Studies were conducted at ATS Labs, located at 1285 Corporate Center Drive, Suite 110, in Eagan, MN 55121.

This data package contained a letter from the applicant's representative to EPA dated August 03, 2012 (MRID 489041-00), EPA Form 8570-4 (CSF), two studies (MRID 489041-06 and 489041-07), proposed label, and Statement of No Data Confidentiality Claims for both studies.

II. USE DIRECTIONS:

The product is designed for disinfection use in water including re-circulating cooling water towers, mechanical or electrolytic generators of chlorine dioxide, potable water treatment, industrial cooling water treatment, mollusk control in water systems, food plant process water treatment, wastewater treatment, paper mills, poultry processing water, oil wells, and petroleum systems.

Directions on the proposed label provide the following information regarding use of the product as a disinfectant for potable water treatment:

Chlorine dioxide is used as both an oxidant and a disinfectant in drinking water treatment. The required dosages will vary with source water conditions and the degree of contamination present. For most municipal and public potable water systems, a chlorine dioxide residual concentration of up to 2 ppm is sufficient to provide adequate disinfection. Residual disinfectant byproducts must be monitored as required by the National Primary Drinking Water Regulation (40 CFR Part 141) and state drinking water standards.

Directions on the proposed label provide the following information regarding use of the product as a disinfectant for food plant process water treatment:

Chlorine dioxide generated from sodium chlorite is effective for use in controlling microbiological growth in flume water and other food processing water systems such as chill water systems and hydro coolers. The required dosages will vary with process conditions and the degree of contamination present. Depending on the requirements of the specific water system, sodium chlorite should be applied continuously or intermittently through a chlorine dioxide generating system to achieve a chlorine dioxide residual concentration between 0.25 and 5.0 ppm.

Water containing up to 3 ppm residual chlorine dioxide may be used for washing fruits and vegetables that are not raw agricultural commodities in accordance with 21CFR§173.300. Treatment of the fruits and vegetables with chlorine dioxide must be followed by a potable water rinse, or by blanching, cooking or canning.

Chlorine dioxide gas may be used for fumigating fruits and vegetables that are not raw agricultural commodities in accordance with 21CFR§173.300. Treatment of the fruits and vegetables with chlorine dioxide in a closed chamber system must be followed by a potable water rinse, or by blanching, cooking or canning.

Directions on the proposed label provide the following information regarding use of the product as a disinfectant for waste water treatment:

Chlorine dioxide is used as both an oxidant and a disinfectant in drinking water treatment. The required dosages will vary with source water conditions and the degree of contamination present. For most municipal and public potable water systems, a chlorine dioxide residual concentration of up to 5 ppm is sufficient to provide adequate disinfection.

For sulfide odor control, between pH 5 – 9, a minimum of 5.2 ppm (wt.) of chlorine dioxide should be applied to oxidize 1 ppm of sulfide (measured as sulfide ion). For phenol destruction, at pH less than 8, 1.5 ppm chlorine dioxide will oxidize 1 ppm phenol; at pH greater than 10, 3.3 ppm chlorine dioxide will oxidize 1 ppm phenol.

Directions on the proposed label provide the following information regarding use of the product as a disinfectant for poultry processing water:

Chlorine dioxide generated from this product may be used as an antimicrobial agent in water used in poultry processing, provided that the residual concentration of chlorine dioxide does not exceed 3 ppm, as determined by an appropriate method in accordance with 21CFR§173.300.

For treatment of poultry chill water, apply this product as necessary through a chlorine dioxide generation system to maintain a residual concentration of up to 3 parts per million (ppm) chlorine dioxide in the chiller water.

Directions on the proposed label provide the following information regarding use of the product as a disinfectant for oil wells and petroleum systems:

Chlorine dioxide is effective in the remediation of bacterial and sulfide contamination commonly found in oilfield production, injection, and disposal fluids. The required dosages will vary with process conditions. Sodium chlorite may be applied either continuously or intermittently through a chlorine dioxide generating system to oil well production water as it is separated from the oil, and before it is re-injected into the well.

For continuous feeds, chlorine dioxide may be applied at dosages slightly higher than sulfide's oxidative demand as determined by a demand study. For intermittent treatment, chlorine dioxide should be applied at a shock dosage of 200 – 3000 ppm.

III. AGENCY STANDARDS FOR PROPOSED CLAIMS:

Products for Treating Water Systems (Emergency water supplies or Water purifier):

These requirements apply to chemical additives such as solutions, powders, or tablets intended for emergency purification of small quantities of drinking water of questionable potability, by the general public, in the absence of bacteriological monitoring facilities. Three samples of product, representing three batches, one of which should be at least 60 days aged, should be tested in triplicate. The "recommended test method" is "Guide Standard and Protocol for Testing Microbiological Water Purifiers - Section 3." This reference is a general guide and in some cases may present only the minimum features and framework for the testing of microbiological water purifiers. However, the principles and approaches outlined in this reference should provide initial

guidance for the testing of various types of units and/or systems for the microbiological purification of contaminated water.

Products must be tested and demonstrated to meet the following microbiological reduction requirements:

- Bacteria: A 6-log (99.9999%) reduction of an influent challenge of 10^7 organisms per 100 mL of the bacterial challenge organism, *Raoultella terrigena* (ATCC 33257).

- Viruses: A 4-log (99.99%) reduction of a mixed influent challenge of 10^7 organisms per liter of each of the following viruses: Poliovirus (LSc) (ATCC VR-59) and Rotavirus (WA or SA-11) (ATCC VR-899 or VR-2018). [Virus types are to be mixed in roughly equal 1 x 10^7/L concentrations and a joint 4 log reduction will be acceptable.]

IV. COMMENTS ON THE SUBMITTED EFFICACY STUDY:

1. MRID 489041-06 "Test Method for Disinfectants for Use in Water," Test Organism: *Raoultella terrigena* (ATCC 33257), for product Technical Sodium Chlorite, by Anne Stemper. Study conducted at ATS Labs 1285 Corporate Center Drive Suite 110 Eagen, MN. 55121. Study completion date – August 3, 2012. Project Identification Number A13273.

This study was conducted against *Raoultella terrigena* (ATCC 33257). Three lots of pure chlorine dioxide stock solution (31% Technical Sodium Chlorite), Lots 20111025, Lot 20120204A, and Lot 20120204B, of the product were tested using the provided ATS Laboratory Protocol No. CWA01122911.CUST.2 marked as proprietary Information. The product lots testing substance were prepared by the sponsor, Lot 20120204A concentration of chlorine dioxide was 350 ppm, Lot 20120204B concentration of chlorine dioxide was 296 ppm, and Lot 20111025 concentration of chlorine dioxide was 755 ppm. For each lot, on the day of testing the sponsor prepared the test substance by bubbling nitrogen gas through the pure chlorine dioxide stock solution and the endpoint determined visually. The sponsor determined the actual chlorine dioxide concentration for each lot by titration and the value (296 – 755 ppm) was used to prepare the 2 ppm chlorine dioxide concentration used in testing. A culture of the challenge microorganism was prepared by streaking an appropriate number of Tryptic Soy + 5% Sheep Blood Agar plates using a stock culture and incubating the plates for 2 days at 35 – 37°C aerobically. Following incubation, the test organism was transferred to Butterfield's Buffer to yield a uniform culture suspension that was adjusted as needed to match a 4.0 McFarland standard. The test water (EPA #2) was prepared by adding 0.60 g sample of dry-autoclaved ISO A2 fine test dust to 500 mL of deionized water and shaken vigorously. In addition, 1.10 g sample of Spectrum humic acid was added to the suspension and shaken vigorously prior to addition of 40 g sample of Sigma sea salts that were mixed vigorously until dissolved. The well mixed suspension was added to a large vessel containing deionized water and mixed thoroughly. The pH of the final test water solution was adjusted as necessary using 10 drops of NaOH to a final pH of 9.04 and the temperature of the EPA #2 water was maintained at 4 ± 1°C (3.5°C) during testing using a water bath set at the desired temperature. The EPA #2 water was prepared within one week of use in testing and was stored at 2 – 8°C. One liter (1000mL) of EPA# 2 test water was inoculated with 2 mL of prepared test organism to target ≥1 X 10^5 CFU per mL or ≥1 X 10^8 CFU per liter and mixed well to ensure the test organism suspension was evenly dispersed. For Lot 20120204A, a 6 mL aliquot of test

substance was added to an inoculated vessel of EPA #2 test water. For Lot 20120204B, a 7 mL aliquot of test substance was added to an inoculated vessel of EPA #2 test water. For Lot 20111025, a 3 mL aliquot of test substance was added to an inoculated vessel of EPA #2 test water. Each sample was thoroughly mixed and allowed to be exposed for 60 minutes at 4 ± 1°C (3.5°C). Two individual 100 mL aliquots of exposed test substance were transferred to vessels containing 10 mL of appropriate neutralizer (0.1 N Sodium Thiosulfate) and mixed. The neutralized sample was filtered through a sterile 0.45 µm filter apparatus system. The filter was rinsed, aseptically removed, and transferred to the surface of Tryptic Soy + 5% Sheep Blood Agar. All subculture plates were incubated for 48 ± 4 hours at 35 – 37°C and stored at 2 – 8°C for three days prior to visual examination for the presence or absence of growth. Controls included purity, sterility, initial suspension population, and neutralization.

2. MRID 489041-07 "Test Method for Disinfectants for the Evaluation of a Water Treatment Product to Reduce Poliovirus type 1 and Rotavirus in Point -of- Use Water," Test Organism: Poliovirus type 1 (ATCC VR 1562) and Rotavirus (University of Ottawa, Ontario Canada), for product Technical Sodium Chlorite, by Mary J. Miller. Study conducted at ATS Labs 1285 Corporate Center Drive Suite 110 Eagen, MN. 55121. Study completion date – July 25, 2012. Project Identification Number A13266.

This study was conducted against Poliovirus type 1, Strain Chat (ATCC VR 1562) and Rotavirus, strain WA (University of Ottawa, Ontario Canada). Rhesus monkey kidney (MA-104) cells were used as the host cell line for both test viruses. Three lots of pure chlorine dioxide stock solution (31% Technical Sodium Chlorite), Lots 20111025, Lot 20120204A, and Lot 20120204B, of the product were tested using the provided ATS Laboratory Protocol No. CWA01122911.CUST.2 marked as proprietary Information. The product lots were received as stock sodium chlorite solutions and added to water for a final concentration of 2 ppm chlorine dioxide for testing. The stock viruses were prepared by collecting the supernatant culture fluid from 75 - 100% infected culture cells that were disrupted and cell debris removed by centrifugation. The high titer stock virus supernatant for each virus were aliquoted and stored at ≤-70°C until the day of use then fifteen (15) aliquots of stock virus for Poliovirus type 1 (ATS Labs Lot PC2-18) and fifteen (15) aliquots of stock virus for Rotavirus (ATS Labs Lot XR-140) were removed, thawed, combined, and maintained at a refrigerated temperature until used in the assay. The test water (EPA #2) was prepared by adding 0.60 g sample of dry-autoclaved ISO A2 fine test dust to 500 mL of deionized water and shaken vigorously. In addition, 1.10 g sample of Spectrum humic acid was added to the suspension and shaken vigorously prior to addition of 40 g sample of Sigma sea salts that were mixed vigorously until dissolved. The well mixed suspension was added to a large vessel containing deionized water and mixed thoroughly. The pH of the final test water solution was adjusted as necessary using 10 drops of NaOH to a final pH of 9.04 and the temperature of the EPA #2 water was maintained at 4 ± 1°C (3.5°C) during testing using a water bath set at the desired temperature. The EPA #2 water was prepared within one week of use in testing and was stored at 2 – 8°C. One liter (1000mL) of EPA# 2 test water for each viral (Rotavirus and Poliovirus type 1) testing were inoculated with 5 mL of virus that had a minimum titer of approximately 1 X 10^7 $TCID_{50}$/mL and mixed well to ensure the test organism suspension was evenly dispersed. Ten-fold serial dilutions were performed from a 5 mL aliquot of the inoculated water to determine the level of virus contained in test water. For Lot 20120204A, a 6 mL aliquot of test substance was added to an inoculated vessel of EPA #2 test water for each virus. For Lot 20120204B,

a 7 mL aliquot of test substance was added to an inoculated vessel of EPA #2 test water for each virus. For Lot 20111025, a 3 mL aliquot of test substance was added to an inoculated vessel of EPA #2 test water for each virus. Each sample was thoroughly mixed and allowed to be exposed for 60 minutes at 4°C. Two individual 10 mL aliquots of exposed test substance were transferred to vessels containing 100 mL of appropriate neutralizer (0.1 N Sodium Thiosulfate) and mixed. Ten-fold (10) serial dilutions were prepared. MA-104 cells in multi well (12 well) culture plates were inoculated in quadruplicate with 1000 µL aliquots of the dilutions prepared from the test and control groups. All subculture plates were incubated at 36 – 38°C with 5 – 7% CO_2 humidified atmosphere. The cultures were score periodically for seven days for the absence or presence of cytopathy, cytotoxicity, and viability. Controls included input virus control, initial virus control, cytotoxicity, and neutralization. Titers were calculated using the Spearman Karber method.

V. RESULTS:

MRID Number	Organism	Geometric Mean and Average Log_{10}			Initial Suspension Population Control Log (CFU/L)
		Lot 20120204A	Lot 20120204B	Lot 20111025	
	60-Minute Exposure Time				
489041-06	*Raoultella terrigena*	<1.00 <0.00	<1.00 <0.00	<1.00 <0.00	1.11×10^9
	Percent Reduction	>99.999999	>99.9999999	>99.9999999	
	Log_{10} Reduction	>8.87	>9.04	>9.23	

MRID Number	Organism	Average $TCID_{50}$/ 1000µL (Log)			Initial Virus Control Average Log_{10} ($TCID_{50}$/1000µL)
		Lot 20120204A	Lot 20120204B	Lot 20111025	
	60-Minute Exposure Time				
489041-07	Poliovirus type 1	$10^{1.07}$	$10^{1.00}$	$10^{1.07}$	$\geq 10^{8.16}$
	Cytotoxicity	None	None	None	
	Joint Initial Control Average	$\geq 10^{8.17}$	$\geq 10^{8.17}$	$\geq 10^{8.17}$	
	Log_{10} Reduction	≥7.09	≥7.16	≥7.09	

MRID Number	Organism	Average $TCID_{50}$/ 1000µL (Log)			Initial Virus Control Average Log_{10} ($TCID_{50}$/1000µL)
		Lot 20120204A	Lot 20120204B	Lot 20111025	
	60-Minute Exposure Time				
489041-07	Rotavirus	$10^{1.39}$	$10^{1.52}$	$10^{1.52}$	$\geq 10^{6.55}$
	Cytotoxicity	None	None	None	
	Joint Initial Virus Control	$\geq 10^{8.17}$	$\geq 10^{8.17}$	$\geq 10^{8.17}$	
	Log_{10} Reduction	5.16	5.03	5.03	

VI. CONCLUSIONS:

1. The submitted efficacy data do not support the use of the product, Technical Sodium Chlorite, as a disinfectant for use in water against the following microorganisms for a 60-minute contact time:

Raoultella terrigena	MRID 489041-06
Poliovirus type 1	MRID 489041-07
Rotavirus	MRID 489041-07

A Lot ≥60 days aged was not tested or clearly indicated in any of the submitted studies. The product identity tested, Pure Chlorine Dioxide Solution (31% Technical Sodium Chlorite), was not confirmed as the product seeking registration, Technical Sodium Chlorite 80% tablet. A 6-log (99.9999%) reduction of an influent challenge of 10^7 organisms per 100 mL of the bacterial challenge organism, *Raoultella terrigena* (ATCC 33257) was demonstrated. A 4-log (99.99%) reduction of a mixed influent challenge of 10^7 organisms per liter of each of the following viruses: Poliovirus and Rotavirus (WA or SA-11) was demonstrated. For MRID 489041-06, purity controls showed pure, sterility controls did not have growth, and neutralization controls demonstrated growth. For MRID 489041-07, there was not any cytotoxicity seen and neutralization controls demonstrated growth.

VII. RECOMMENDATIONS:

1. The proposed label claims that the product, Technical Sodium Chlorite, is an effective disinfectant for use in water against the following microorganisms for a 60-minute contact time:

Raoultella terrigena	ATCC 33257
Poliovirus type 1	ATCC VR-1562
Rotavirus, Strain WA	University of Ottawa, Ontario Canada

These claims are **unacceptable** as they are not supported by the submitted data.

2. The following recommendations for the **Label** must be made:

- The dilution rate must be indicated. Directions for use must include the dilution of the product needed to accomplish the indicated ppm for each usage.
- In order to add claims using the registration eligibility decision (RED), an available chlorine test must be performed to determine the product equivalence to the established ppm level that demonstrates efficacy for RED claims.